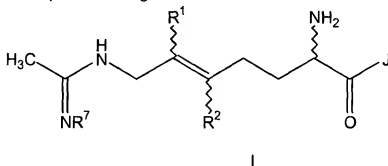


WHAT IS CLAIMED IS:

1. A method for the treatment or prevention of conditions or diseases of the gastrointestinal tract involving an overproduction of nitric oxide (NO) by inducible nitric oxide synthase (iNOS), in a subject in need of such treatment or prevention, said method comprising administering to the subject an anti-inflammatory effective amount of an inducible nitric oxide synthase selective inhibitor or pharmaceutically acceptable salt thereof or prodrug thereof, wherein the inducible nitric oxide synthase inhibitor is selected from the group consisting of:  
a compound having Formula I



15

wherein:

R<sup>1</sup> is selected from the group consisting of H, halo and alkyl which may be optionally substituted by one or more halo;

- R<sup>2</sup> is selected from the group consisting of H, halo and alkyl which may be optionally substituted by one or more halo;  
with the proviso that at least one of R<sup>1</sup> or R<sup>2</sup> contains a halo;

R<sup>7</sup> is selected from the group consisting of H and hydroxy;

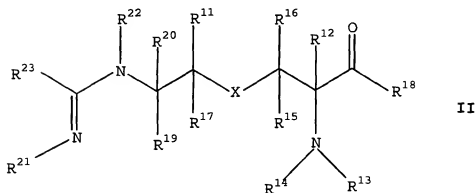
J is selected from the group consisting of hydroxy, alkoxy, and NR<sup>3</sup>R<sup>4</sup>

- 25 wherein;

R<sup>3</sup> is selected from the group consisting of H, lower alkyl, lower alkynyl and lower alkynyl;

R<sup>4</sup> is selected from the group consisting of H, and a heterocyclic ring in which at least one member of the ring is carbon and in which 1 to about 4 heteroatoms are independently selected from oxygen, nitrogen and sulfur and said heterocyclic ring may be optionally substituted with heteroarylamino, N-aryl-N-alkylamino, N-heteroarylamino-N-alkylamino, haloalkylthio, alkanoyloxy, alkoxy, heteroaralkoxy, cycloalkoxy, cycloalkenyloxy, hydroxy, amino, thio, nitro, lower alkylamino, alkylthio, alkylthioalkyl, arylamino, aralkylamino, arylthio, alkylsulfinyl, alkylsulfonyl, alkylsulfonamido, alkylaminosulfonyl, amidosulfonyl, monoalkyl amidosulfonyl, dialkyl amidosulfonyl, monoarylamidosulfonyl, arylsulfonamido, diarylamidosulfonyl, monoalkyl monoaryl amidosulfonyl, arylsulfinyl, arylsulfonyl, heteroarylthio, heteroarylsulfinyl, heteroarylsulfonyl, alkanoyl, alkenoyl, aroyl, heteroaroyl, aralkanoyl, heteroaralkanoyl, haloalkanoyl, alkyl, alkenyl, alkynyl, alkylenedioxy, haloalkylenedioxy, cycloalkyl, cycloalkenyl, lower cycloalkylalkyl, lower cycloalkenylalkyl, halo, haloalkyl, haloalkoxy, hydroxyhaloalkyl, hydroxyaralkyl, hydroxyalkyl, hydroxyheteroaralkyl, haloalkoxyalkyl, aryl, aralkyl, aryloxy, aralkoxy, aryloxyalkyl, saturated heterocyclyl, partially saturated heterocyclyl, heteroaryl, heteroaryloxy, heteroaryloxyalkyl, arylalkyl, heteroarylalkyl, arylalkenyl, heteroarylalkenyl, cyanoalkyl, dicyanoalkyl, carboxamidoalkyl, dicarboxamidoalkyl, cyanocarboalkoxyalkyl, carboalkoxyalkyl, dicarboalkoxyalkyl, cyanocycloalkyl, dicyanocycloalkyl, carboxamidocycloalkyl, dicarboxamidocycloalkyl, carboalkoxycyanocycloalkyl, carboalkoxycycloalkyl, dicarboalkoxycycloalkyl, formylalkyl, acylalkyl, dialkoxyphosphonoalkyl, diaralkoxyphosphonoalkyl, phosphonoalkyl, dialkoxyphosphonoalkoxy, diaralkoxyphosphonoalkoxy, phosphonoalkoxy, dialkoxyphosphonoalkylamino, diaralkoxyphosphonoalkylamino, phosphonoalkylamino, dialkoxyphosphonoalkyl, diaralkoxyphosphonoalkyl, guanidino, amidino, and acylamino;

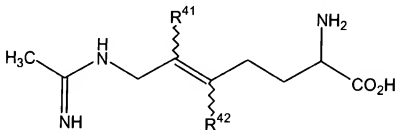
a compound having a structure corresponding to Formula II



- wherein X is selected from the group consisting of -S-, -S(O)-, and -S(O)<sub>2</sub>-, R<sup>12</sup> is selected from the group consisting of C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>2</sub>-C<sub>6</sub> alkenyl, C<sub>2</sub>-C<sub>6</sub> alkynyl, C<sub>1</sub>-C<sub>6</sub> alkoxy-C<sub>1</sub> alkyl, and C<sub>1</sub>-C<sub>6</sub> alkylthio-C<sub>1</sub> alkyl wherein each of these groups is optionally substituted by one or more substituent selected from the group consisting of -OH, alkoxy, and halogen, R<sup>18</sup> is selected from the group consisting of -OR<sup>24</sup> and -N(R<sup>25</sup>)(R<sup>26</sup>), and R<sup>13</sup> is selected from the group consisting of -H, -OH, -C(O)-R<sup>27</sup>, -C(O)-O-R<sup>28</sup>, and -C(O)-S-R<sup>29</sup>; or R<sup>18</sup> is -N(R<sup>30</sup>)-, and R<sup>13</sup> is -C(O)-, wherein R<sup>18</sup> and R<sup>13</sup> together with the atoms to which they are attached form a ring; or R<sup>18</sup> is -O-, and R<sup>13</sup> is -C(R<sup>31</sup>)(R<sup>32</sup>)-, wherein R<sup>18</sup> and R<sup>13</sup> together with the atoms to which they are attached form a ring, wherein if R<sup>13</sup> is -C(R<sup>31</sup>)(R<sup>32</sup>)-, then R<sup>14</sup> is -C(O)-O-R<sup>33</sup>; otherwise R<sup>14</sup> is -H, R<sup>11</sup>, R<sup>15</sup>, R<sup>16</sup>, and R<sup>17</sup> independently are selected from the group consisting of -H, halogen, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>2</sub>-C<sub>6</sub> alkenyl, C<sub>2</sub>-C<sub>6</sub> alkynyl, and C<sub>1</sub>-C<sub>6</sub> alkoxy-C<sub>1</sub> alkyl, R<sup>19</sup> and R<sup>20</sup> independently are selected from the group consisting of -H, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>2</sub>-C<sub>6</sub> alkenyl, C<sub>2</sub>-C<sub>6</sub> alkynyl, and C<sub>1</sub>-C<sub>6</sub> alkoxy-C<sub>1</sub> alkyl, R<sup>21</sup> is selected from the group consisting of -H, -OH, -C(O)-O-R<sup>34</sup>, and -C(O)-S-R<sup>35</sup>, and R<sup>22</sup> is selected from the group consisting of -H, -OH, -C(O)-O-R<sup>36</sup>, and -C(O)-S-R<sup>37</sup>; or R<sup>21</sup> is -O-, and R<sup>22</sup> is -C(O)-, wherein R<sup>21</sup> and R<sup>22</sup> together with the atoms to which they are attached form a ring; or R<sup>21</sup> is -C(O)-, and R<sup>22</sup> is -O-, wherein R<sup>21</sup> and R<sup>22</sup>

together with the atoms to which they are attached form a ring,  $R^{23}$  is C, alkyl,  $R^{24}$  is selected from the group consisting of -H and  $C_1$ - $C_6$  alkyl, wherein when  $R^{24}$  is  $C_1$ - $C_6$  alkyl,  $R^{24}$  is optionally substituted by one or more moieties selected from the group consisting of cycloalkyl, heterocyclyl, aryl, and heteroaryl,  $R^{25}$  is selected from the group consisting of -H, alkyl, and alkoxy, and  $R^{26}$  is selected from the group consisting of -H, -OH, alkyl, alkoxy,  $-C(O)-R^{38}$ ,  $-C(O)-O-R^{39}$ , and  $-C(O)-S-R^{40}$ ; wherein when  $R^{25}$  and  $R^{26}$  independently are alkyl or alkoxy,  $R^{25}$  and  $R^{26}$  independently are optionally substituted with one or more moieties selected from the group consisting of cycloalkyl, heterocyclyl, aryl, and heteroaryl; or  $R^{25}$  is -H; and  $R^{26}$  is selected from the group consisting of cycloalkyl, heterocyclyl, aryl, and heteroaryl,  $R^{27}$ ,  $R^{28}$ ,  $R^{29}$ ,  $R^{30}$ ,  $R^{31}$ ,  $R^{32}$ ,  $R^{33}$ ,  $R^{34}$ ,  $R^{35}$ ,  $R^{36}$ ,  $R^{37}$ ,  $R^{38}$ ,  $R^{39}$ , and  $R^{40}$  independently are selected from the group consisting of -H and alkyl, wherein alkyl is optionally substituted by one or more moieties selected from the group consisting of cycloalkyl, heterocyclyl, aryl, and heteroaryl, wherein when any of  $R^{11}$ ,  $R^{12}$ ,  $R^{13}$ ,  $R^{14}$ ,  $R^{15}$ ,  $R^{16}$ ,  $R^{17}$ ,  $R^{18}$ ,  $R^{19}$ ,  $R^{20}$ ,  $R^{21}$ ,  $R^{22}$ ,  $R^{23}$ ,  $R^{24}$ ,  $R^{25}$ ,  $R^{26}$ ,  $R^{27}$ ,  $R^{28}$ ,  $R^{29}$ ,  $R^{30}$ ,  $R^{31}$ ,  $R^{32}$ ,  $R^{33}$ ,  $R^{34}$ ,  $R^{35}$ ,  $R^{36}$ ,  $R^{37}$ ,  $R^{38}$ ,  $R^{39}$ , and  $R^{40}$  independently is a moiety selected from the group consisting of alkyl, alkenyl, alkynyl, alkoxy, alkylthio, cycloalkyl, heterocyclyl, aryl, and heteroaryl, then the moiety is optionally substituted by one or more substituent selected from the group consisting of -OH, alkoxy, and halogen;

a compound represented by Formula III



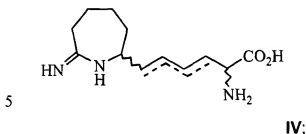
III

wherein:

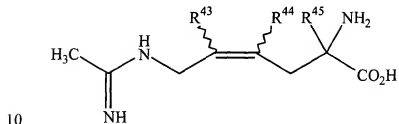
$R^{41}$  is H or methyl; and

$R^{42}$  is H or methyl;

a compound of formula **IV**



a compound of Formula **V**:



**V**

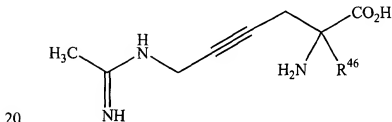
wherein:

$R^{43}$  is selected from the group consisting of hydrogen, halo,  $C_1$ - $C_8$  alkyl and  $C_1$ - $C_8$  alkyl substituted by alkoxy or one or more halo;

15  $R^{44}$  is selected from the group consisting of hydrogen, halo,  $C_1$ - $C_8$  alkyl and  $C_1$ - $C_8$  alkyl substituted by alkoxy or one or more halo;

$R^{45}$  is  $C_1$ - $C_8$  alkyl or  $C_1$ - $C_8$  alkyl substituted by alkoxy or one or more halo;

a compound of Formula **VI**:

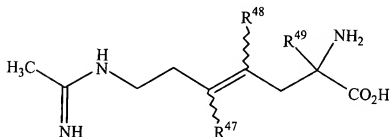


# VI

wherein:

$R^{46}$  is  $C_1$ - $C_5$  alkyl, said  $C_1$ - $C_5$  alkyl optionally substituted by halo or alkoxy, said alkoxy optionally substituted by one or more halo;

5 a compound of Formula VII



# VII

10 wherein:

$R^{47}$  is selected from the group consisting of hydrogen, halo,  $C_1$ - $C_5$  alkyl and  $C_1$ - $C_5$  alkyl substituted by alkoxy or one or more halo;

$R^{48}$  is selected from the group consisting of hydrogen, halo,  $C_1$ - $C_5$  alkyl and  $C_1$ - $C_5$  alkyl substituted by alkoxy or one or more halo;

15  $R^{49}$  is  $C_1$ - $C_5$  alkyl or  $C_1$ - $C_5$  alkyl be substituted by alkoxy or one or more halo;  
a compound of Formula VIII

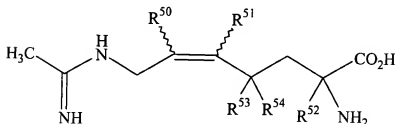


# VIII

20 wherein:

$R^{50}$  is  $C_1$ - $C_5$  alkyl, said  $C_1$ - $C_5$  alkyl optionally substituted by halo or alkoxy, said alkoxy optionally substituted by one or more halo;

a compound of formula IX



IX

wherein:

$R^{50}$  is selected from the group consisting of hydrogen, halo, and  $C_1$ - $C_5$  alkyl, said  $C_1$ - $C_5$  alkyl optionally substituted by halo or alkoxy, said alkoxy optionally substituted by one or more halo;

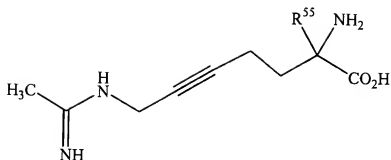
$R^{51}$  is selected from the group consisting of hydrogen, halo, and  $C_1$ - $C_5$  alkyl, said  $C_1$ - $C_5$  alkyl optionally substituted by halo or alkoxy, said alkoxy optionally substituted by one or more halo;

$R^{52}$  is  $C_1$ - $C_5$  alkyl, said  $C_1$ - $C_5$  alkyl optionally substituted by halo or alkoxy, said alkoxy optionally substituted by one or more halo;

$R^{53}$  is selected from the group consisting of hydrogen, halo, and  $C_1$ - $C_5$  alkyl, said  $C_1$ - $C_5$  alkyl optionally substituted by halo or alkoxy, said alkoxy optionally substituted by one or more halo; and

$R^{54}$  is selected from the group consisting of halo and  $C_1$ - $C_5$  alkyl, said  $C_1$ - $C_5$  alkyl optionally substituted by halo or alkoxy, said alkoxy optionally substituted by one or more halo;

a compound of formula X

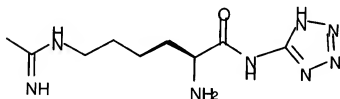


**X**

wherein:

- $R^{55}$  is  $C_1$ - $C_5$  alkyl, said  $C_1$ - $C_5$  alkyl optionally substituted by halo or alkoxy,  
5 said alkoxy optionally substituted by one or more halo.

*a compound having the formula XI*

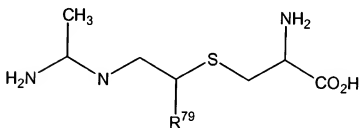


- 10 2S-amino-6-[(1-iminoethyl)amino]-N-(1H-tetrazol-5-yl) hexanamide, hydrate,  
dihydrochloride

**XI**

A compound of formula XII:

15

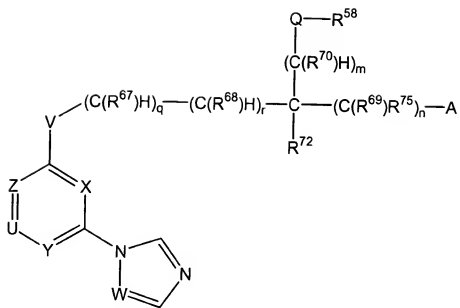


**XII**

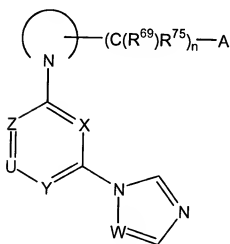
- wherein  $R^{79}$  is selected from  $C_{1-4}$  alkyl,  $C_{3-4}$  cycloalkyl,  $C_{1-4}$  hydroxyalkyl,  
20 and  $C_{1-4}$  haloalkyl;

a compound of Formula XIII, Formula XIV or Formula XV:

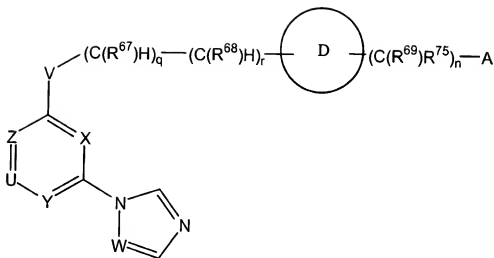




Formula XIII;



Formula XIV; or



Formula XV;

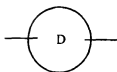
wherein:

- 5 A is  $-R^{56}$ ,  $-OR^{56}$ ,  $C(O)N(R^{56})R^{57}$ ,  $P(O)[N(R^{56})R^{57}]_2$ ,  $-N(R^{56})C(O)R^{57}$ ,  $-N(R^{76})C(O)OR^{56}$ ,  $-N(R^{56})R^{76}$ ,  $-N(R^{71})C(O)N(R^{56})R^{71}$ ,  $-S(O)_2R^{56}$ ,  $-SO_2NHC(O)R^{56}$ ,  $-NHSO_2R^{77}$ ,  $-SO_2NH(R^{56})H$ ,  $-C(O)NHSO_2R^{77}$ , and  $-CH=NOR^{56}$ ;
- 10 each X, Y and Z are independently N or  $C(R^{19})$ ;
- each U is N or  $C(R^{60})$ , provided that U is N only when X is N and Z and Y are  $CR^{74}$ ;
- V is  $N(R^{59})$ , S, O or  $C(R^{59})H$ ;
- Each W is N or CH;
- Q is chosen from the group consisting of a direct bond,  $-C(O)-$ ,  $-O-$ ,  $-C(=N-R^{56})-$ ,  $S(O)_2$ , and  $-N(R^{61})-$ ;
- 15 m is zero or an integer from 1 to 4;
- n is zero or an integer from 1 to 3;
- q is zero or one;
- r is zero or one, provided that when Q and V are heteroatoms, m, q, and r
- 20 cannot all be zero;

- when A is  $-\text{OR}^{56}$ ,  $\text{N}(\text{R}^{56})\text{C}(\text{O})\text{R}^{57}$ ,  $-\text{N}(\text{R}^{71})\text{C}(\text{O})\text{OR}^{57}$ ,  $-\text{N}(\text{R}^{56})\text{R}^{76}$ ,  $-\text{N}(\text{R}^{71})\text{C}(\text{O})\text{N}(\text{R}^{56})\text{R}^{71}$ ,  $-\text{S}(\text{O})_t\text{R}^{56}$  (where t is zero), or  $-\text{NHSO}_2\text{R}^{77}$ , n, q, and r cannot all be zero; and when Q is a heteroatom and A is  $-\text{OR}^{56}$ ,  $\text{N}(\text{R}^{56})\text{C}(\text{O})\text{R}^{57}$ ,  $-\text{N}(\text{R}^{71})\text{C}(\text{O})\text{OR}^{57}$ ,  $-\text{N}(\text{R}^{56})\text{R}^{76}$ ,  $\text{N}(\text{R}^{71})\text{C}(\text{O})\text{N}(\text{R}^{56})\text{R}^{71}$ ,  $-\text{S}(\text{O})_t\text{R}^{56}$  (when t is zero), or  $-\text{NHSO}_2\text{R}^{77}$ , m and n cannot both be zero; t is zero, one or two;



is an optionally substituted N-heterocyclyl;



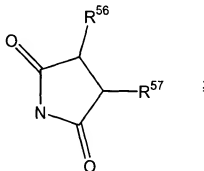
- 10 is an optionally substituted carbocyclyl or optionally substituted N-heterocyclyl;

- each  $\text{R}^{56}$  and  $\text{R}^{57}$  are independently chosen from the group consisting of hydrogen, optionally substituted  $\text{C}_1\text{-C}_{20}$  alkyl, optionally substituted cycloalkyl,  $-\text{[C}_0\text{-C}_8\text{ alkyl]}\text{-R}^{64}$ ,  $-\text{[C}_2\text{-C}_8\text{ alkenyl]}\text{-R}^{64}$ ,  $-\text{[C}_2\text{-C}_8\text{ alkynyl]}\text{-R}^{64}$ ,  $-\text{[C}_2\text{-C}_8\text{ alkyl]}\text{-R}^{65}$  (optionally substituted by hydroxy),  $-\text{[C}_1\text{-C}_6\text{ ]}\text{-R}^{66}$  (optionally substituted by hydroxy), optionally substituted heterocyclyl;

or  $\text{R}^{56}$  and  $\text{R}^{57}$  together with the nitrogen atom to which they are attached is an optionally substituted N-heterocyclyl;

- $\text{R}^{58}$  is chosen from the group consisting of hydrogen, alkyl, cycloalkyl, 20 optionally substituted aryl, haloalkyl,  $-\text{[C}_1\text{-C}_8\text{ alkyl]}\text{-C}(\text{O})\text{N}(\text{R}^{56})\text{R}^{57}$ ,  $-\text{[C}_1\text{-C}_8\text{ alkyl]}\text{-N}(\text{R}^{56})\text{R}^{57}$ ,  $-\text{[C}_1\text{-C}_8\text{ alkyl]}\text{-R}^{63}$ ,  $-\text{[C}_2\text{-C}_8\text{ alk2yl]}\text{-R}^{65}$ ,  $-\text{[C}_1\text{-C}_8\text{ alkyl]}\text{-R}^{66}$ , and heterocyclyl (optionally substituted by one or more substituents selected from the group consisting of halo, alkyl, alkoxy and imidazolyl);

- or when Q is  $-N(R^{56})-$  or a direct bond to  $R^{56}$ ,  $R^{56}$  may additionally be aminocarbonyl, alkoxy carbonyl, alkylsulfonyl, monoalkylaminocarbonyl, dialkylaminocarbonyl and  $-C(=NR^{73})-NH_2$ ;
- 5 or  $-Q-R^{56}$  taken together represents  $-C(O)OH$ ,  $-C(O)N(R^{56})R^{57}$  or

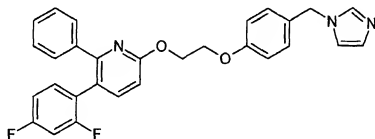


- $R^{59}$  is chosen from the group consisting of hydrogen, alkyl, aryl, aralkyl and cycloalkyl;
- 10 Provided that when A is  $-R^{56}$  or  $-OR^{56}$ ,  $R^{59}$  cannot be hydrogen, and when V is CH,  $R^{59}$  may additionally be hydroxy;
- $R^{60}$  is chosen from the group consisting of hydrogen, alkyl, aryl, aralkyl, haloalkyl, optionally substituted aralkyl, optionally substituted aryl,  $-OR^{71}$ ,  $-S(O)_2-R^{71}$ ,
- 15  $N(R^{71})R^{76}$ ,  $N(R^{71})C(O)N(R^{56})R^{71}$ ,  $N(R^{71})C(O)OR^{71}$ ,  $N(R^{71})C(O)R^{71}$ ,  $-[C_6-C_8 \text{ alkyl}]-C(H)[C(O)R^{71}]_2$  and  $-[C_6-C_8 \text{ alkyl}]-C(O)N(R^{56})R^{71}$ ;
- $R^{61}$  is chosen from the group consisting of hydrogen, alkyl, cycloalkyl,  $-[C_1-C_8 \text{ alkyl}]-R^{63}$ ,  $-[C_2-C_8 \text{ alkyl}]-R^{65}$ ,  $-[C_1-C_8 \text{ alkyl}]-R^{66}$ , acyl,  $-C(O)R^{63}$ ,  $-C(O)-[C_1-C_8 \text{ alkyl}]-R^{63}$ , alkoxy carbonyl, optionally substituted aryloxy carbonyl,
- 20 optionally substituted aralkoxy carbonyl, alkylsulfonyl, optionally substituted aryl, optionally substituted heterocyclyl, alkoxy carbonylalkyl, carboxyalkyl, optionally substituted arylsulfonyl, aminocarbonyl, monoalkylaminocarbonyl, dialkylaminocarbonyl, optionally substituted arylaminocarbonyl, aminosulfonyl,

- monoalkylaminosulfonyl dialkylaminosulfonyl, arylaminosulfonyl, arylsulfonylaminocarbonyl, optionally substituted N-heterocyclyl,  $-\text{C}(=\text{NH})-\text{N}(\text{CN})\text{R}^{56}$ ,  $-\text{C}(\text{O})\text{R}^{78}-\text{N}(\text{R}^{56})\text{R}^{57}$ ,  $-\text{C}(\text{O})-\text{N}(\text{R}^{56})\text{R}^{78}-\text{C}(\text{O})\text{OR}^{56}$ , each  $\text{R}^{63}$  and  $\text{R}^{64}$  are independently chosen from the group consisting of
- 5 haloalkyl, cycloalkyl, (optionally substituted with halo, cyano, alkyl or alkoxy), carbocyclyl (optionally substituted with one or more substituents selected from the group consisting of halo, alkyl and alkoxy) and heterocyclyl (optionally substituted with alkyl, aralkyl or alkoxy);
- 10 each  $\text{R}^{65}$  is independently chosen from the group consisting of halo, alkoxy, optionally substituted aryloxy, optionally substituted aralkoxy, optionally substituted  $-\text{S}(\text{O})_2-\text{R}^{77}$ , acylamino, amino, monoalkylamino, dialkylamino, (triphenylmethyl)amino, hydroxy, mercapto, alkylsulfonamido;
- 15 each  $\text{R}^{66}$  is independently chosen from the group consisting of cyano, di(alkoxy)alkyl, carboxy, alkoxycarbonyl, aminocarbonyl, monoalkylaminocarbonyl and dialkylaminocarbonyl; each  $\text{R}^{67}$ ,  $\text{R}^{68}$ ,  $\text{R}^{69}$ ,  $\text{R}^{70}$ ,  $\text{R}^{72}$ , and  $\text{R}^{75}$  are independently hydrogen or alkyl;
- 20 each  $\text{R}^{71}$  is independently hydrogen, alkyl, optionally substituted aryl, optionally substituted aralkyl or cycloalkyl;  $\text{R}^{73}$  is hydrogen,  $\text{NO}_2$ , or toluenesulfonyl; each  $\text{R}^{74}$  is independently hydrogen, alkyl (optionally substituted with hydroxy), cyclopropyl, halo or haloalkyl;
- 25 each  $\text{R}^{76}$  is independently hydrogen, alkyl, cycloalkyl, optionally substituted aryl, optionally substituted aralkyl,  $-\text{C}(\text{O})\text{R}^{77}$  or  $-\text{SO}_2\text{R}^{77}$ ; or  $\text{R}^{76}$  taken together with  $\text{R}^{56}$  and the nitrogen to which they are attached is an optionally

- substituted N-heterocyclyl;  
or R<sup>76</sup> taken together with R<sup>71</sup> and the nitrogen to which they are attached is an optionally substituted N-heterocyclyl;  
5 each R<sup>77</sup> is independently alkyl, cycloalkyl, optionally substituted aryl or optionally substituted aralkyl; and  
R<sup>78</sup> is an amino acid residue; and

10 PPA250



PPA250

- or a pharmaceutically acceptable salt or prodrug of any of said inducible nitric  
15 oxide synthase inhibitors.

2. The method of claim 1 wherein the condition or disease of the gastrointestinal tract is selected from the group consisting of inflammatory bowel disease, Crohn's disease, ulcerative colitis, peptic ulcer disease, gastric  
20 ulceration, duodenal ulceration, gastritis, ileitis, gastroesophageal reflux disease, irritable bowel syndrome, paralytic ileus and diarrhea.

3. The method of claim 1 wherein the condition or disease of the gastrointestinal tract is inflammatory bowel disease.

4. The method of claim 1 wherein the condition or disease of the gastrointestinal tract is Crohn's disease.
5. The method of claim 1 wherein the condition or disease of the gastrointestinal tract is ulcerative colitis.
- 5 6. The method of claim 1 wherein the condition or disease of the gastrointestinal tract is gastritis.
7. The method of claim 1 wherein the condition or disease of the gastrointestinal tract is ileitis.
8. The method of claim 1 wherein the condition or disease of the  
10 gastrointestinal tract is peptic ulceration.
9. The method of claim 8 wherein the condition or disease of the gastrointestinal tract is gastric ulceration.
10. The method of claim 8 wherein the condition or disease of the gastrointestinal tract is duodenal ulceration.
- 15 11. The method of claim 1 wherein the condition or disease of the gastrointestinal tract is esophagitis.
12. The method of claim 1 wherein the condition or disease of the gastrointestinal tract is gastroesophageal reflux disease.
13. The method of claim 1 wherein the condition or disease of the  
20 gastrointestinal tract is irritable bowel syndrome.
14. The method of Claim 1 wherein the condition or disease of the gastrointestinal tract is selected from group consisting of peptic ulcer disease

and gastritis, said method further comprising administering to the subject an amount of an antimicrobial compound or pharmaceutically acceptable salt thereof or prodrug thereof, wherein the amount of the inducible nitric oxide synthase selective inhibitor and the amount of the antimicrobial compound  
5 together constitute an amount effective against the condition or disease of the gastrointestinal tract.

15. The method of Claim 14 wherein the antimicrobial compound comprises an antibiotic compound.

16. The method of Claim 14 wherein the antimicrobial compound  
10 comprises at least one compound selected from the group consisting of the following: amoxicillin, clarithromycin, rifabutin, bismuth subsalicylate, metronidazole, and tetracycline.

17. The method of Claim 1 further comprising administering to the subject an amount of an antisecretory compound or pharmaceutically  
15 acceptable salt thereof or prodrug thereof, wherein the amount of the inducible nitric oxide synthase selective inhibitor and the amount of the antisecretory compound together constitute an amount effective against the condition or disease of the gastrointestinal tract.1

18. The method of Claim 17 wherein the antisecretory compound  
20 comprises a proton-pump inhibitor.

19. The method of Claim 17 wherein the antisecretory compound comprises omeprazole.

20. The method of Claim 17 wherein the antisecretory compound comprises an H<sub>2</sub>receptor anatagonist.

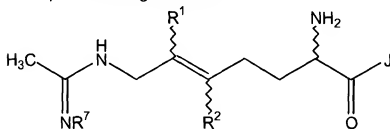
21. The method of Claim 20 wherein the antisecretory compound  
25 comprises ranitidine.

22. A method for the treatment or prevention of inflammatory conditions or diseases of the gastrointestinal tract involving an overproduction of nitric oxide (NO) by inducible nitric (iNOS) and microbial infection, in a  
30 subject in need of such treatment or prevention, said method comprising administering to the subject an amount of



an inducible nitric oxide synthase selective inhibitor or pharmaceutically acceptable salt thereof or prodrug thereof, and an amount of an antimicrobial compound or pharmaceutically acceptable salt thereof or prodrug thereof, wherein the amount of the inducible nitric oxide synthase selective inhibitor and the amount of the antibiotic compound together constitute an amount effective against the condition or disease of the gastrointestinal tract, wherein the inducible nitric oxide synthase inhibitor is selected from the group consisting of:

a compound having Formula I



I

wherein:

R<sup>1</sup> is selected from the group consisting of H, halo and alkyl which may be optionally substituted by one or more halo;

R<sup>2</sup> is selected from the group consisting of H, halo and alkyl which may be optionally substituted by one or more halo;

with the proviso that at least one of R<sup>1</sup> or R<sup>2</sup> contains a halo;

R<sup>7</sup> is selected from the group consisting of H and hydroxy;

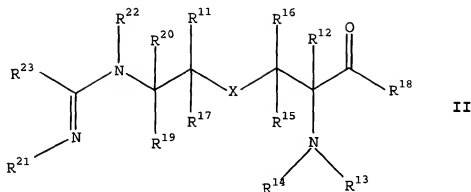
J is selected from the group consisting of hydroxy, alkoxy, and NR<sup>3</sup>R<sup>4</sup> wherein;

R<sup>3</sup> is selected from the group consisting of H, lower alkyl, lower alkynyl and lower alkynyl;

R<sup>4</sup> is selected from the group consisting of H, and a heterocyclic ring in which at least one member of the ring is carbon and in which 1 to about 4

- heteroatoms are independently selected from oxygen, nitrogen and sulfur and said heterocyclic ring may be optionally substituted with heteroaryl-amino, N-aryl-N-alkylamino, N-heteroaryl-amino-N-alkylamino, haloalkylthio, alkanoyloxy, alkoxy, heteroaralkoxy, cycloalkoxy, cycloalkenyloxy, hydroxy, amino, thio,
- 5 nitro, lower alkylamino, alkylthio, alkylthioalkyl, arylamino, aralkylamino, arylthio, alkylsulfinyl, alkylsulfonyl, alkylsulfonamido, alkylaminosulfonyl, amidosulfonyl, monoalkyl amidosulfonyl, dialkyl amidosulfonyl, monoarylamidosulfonyl, arylsulfonamido, diarylamidosulfonyl, monoalkyl monoaryl amidosulfonyl, arylsulfinyl, arylsulfonyl, heteroarylthio,
- 10 heteroarylsulfinyl, heteroarylsulfonyl, alkanoyl, alkenoyl, aroyl, heteroaroyl, aralkanoyl, heteroaralkanoyl, haloalkanoyl, alkyl, alkenyl, alkynyl, alkylenedioxy, haloalkylenedioxy, cycloalkyl, cycloalkenyl, lower cycloalkylalkyl, lower cycloalkenylalkyl, halo, haloalkyl, haloalkoxy, hydroxyhaloalkyl, hydroxyaralkyl, hydroxyalkyl, hydroxyheteroaralkyl, haloalkoxyalkyl, aryl,
- 15 aralkyl, aryloxy, aralkoxy, aryloxyalkyl, saturated heterocyclyl, partially saturated heterocyclyl, heteroaryl, heteroaryloxy, heteroaryloxyalkyl, arylalkyl, heteroarylalkyl, arylalkenyl, heteroarylalkenyl, cyanoalkyl, dicyanoalkyl, carboxamidoalkyl, dicarboxamidoalkyl, cyanocarboalkoxyalkyl, carboalkoxyalkyl, dicarboalkoxyalkyl, cyanocycloalkyl, dicyanocycloalkyl,
- 20 carboxamidocycloalkyl, dicarboxamidocycloalkyl, carboalkoxycyanocycloalkyl, carboalkoxycycloalkyl, dicarboalkoxycycloalkyl, formylalkyl, acylalkyl, dialkoxyphosphonoalkyl, diaralkoxyphosphonoalkyl, phosphonoalkyl, dialkoxyphosphonoalkoxy, diaralkoxyphosphonoalkoxy, phosphonoalkoxy, dialkoxyphosphonoalkylamino, diaralkoxyphosphonoalkylamino,
- 25 phosphonoalkylamino, dialkoxyphosphonoalkyl, diaralkoxyphosphonoalkyl, guanidino, amidino, and acylamino;

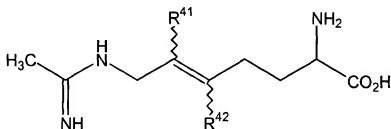
a compound having a structure corresponding to Formula II



- wherein X is selected from the group consisting of -S-, -S(O)-, and -S(O)<sub>2</sub>-, R<sup>12</sup> is selected from the group consisting of C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>2</sub>-C<sub>6</sub> alkenyl, C<sub>2</sub>-C<sub>6</sub> alkynyl, C<sub>1</sub>-C<sub>5</sub> alkoxy-C<sub>1</sub> alkyl, and C<sub>1</sub>-C<sub>5</sub> alkylthio-C<sub>1</sub> alkyl wherein each of these groups is optionally substituted by one or more substituent selected from the group consisting of -OH, alkoxy, and halogen, R<sup>18</sup> is selected from the group consisting of -OR<sup>24</sup> and -N(R<sup>25</sup>)(R<sup>26</sup>), and R<sup>13</sup> is selected from the group consisting of -H, -OH, -C(O)-R<sup>27</sup>, -C(O)-O-R<sup>28</sup>, and -C(O)-S-R<sup>29</sup>; or R<sup>18</sup> is -N(R<sup>30</sup>)-, and R<sup>13</sup> is -C(O)-, wherein R<sup>18</sup> and R<sup>13</sup> together with the atoms to which they are attached form a ring; or R<sup>18</sup> is -O-, and R<sup>13</sup> is -C(R<sup>31</sup>)(R<sup>32</sup>)-, wherein R<sup>18</sup> and R<sup>13</sup> together with the atoms to which they are attached form a ring, wherein if R<sup>13</sup> is -C(R<sup>31</sup>)(R<sup>32</sup>)-, then R<sup>14</sup> is -C(O)-O-R<sup>33</sup>; otherwise R<sup>14</sup> is -H, R<sup>11</sup>, R<sup>15</sup>, R<sup>16</sup>, and R<sup>17</sup> independently are selected from the group consisting of -H, halogen, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>2</sub>-C<sub>6</sub> alkenyl, C<sub>2</sub>-C<sub>6</sub> alkynyl, and C<sub>1</sub>-C<sub>5</sub> alkoxy-C<sub>1</sub> alkyl, R<sup>19</sup> and R<sup>20</sup> independently are selected from the group consisting of -H, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>2</sub>-C<sub>6</sub> alkenyl, C<sub>2</sub>-C<sub>6</sub> alkynyl, and C<sub>1</sub>-C<sub>5</sub> alkoxy-C<sub>1</sub> alkyl, R<sup>21</sup> is selected from the group consisting of -H, -OH, -C(O)-O-R<sup>34</sup>, and -C(O)-S-R<sup>35</sup>, and R<sup>22</sup> is selected from the group consisting of -H, -OH, -C(O)-O-R<sup>36</sup>, and -C(O)-S-R<sup>37</sup>; or R<sup>21</sup> is -O-, and R<sup>22</sup> is -C(O)-, wherein R<sup>21</sup> and R<sup>22</sup> together with the atoms to which they are attached form a ring; or R<sup>21</sup> is -C(O)-, and R<sup>22</sup> is -O-, wherein R<sup>21</sup> and R<sup>22</sup> together with the atoms to which they are attached form a ring, R<sup>23</sup> is C<sub>1</sub> alkyl, R<sup>24</sup> is selected from the group consisting of -H and C<sub>1</sub>-C<sub>6</sub> alkyl, wherein when

$R^{24}$  is C<sub>1</sub>-C<sub>6</sub> alkyl,  $R^{24}$  is optionally substituted by one or more moieties selected from the group consisting of cycloalkyl, heterocyclyl, aryl, and heteroaryl,  $R^{25}$  is selected from the group consisting of -H, alkyl, and alkoxy, and  $R^{26}$  is selected from the group consisting of -H, -OH, alkyl, alkoxy, -C(O)- $R^{38}$ , -C(O)-O- $R^{39}$ , and -C(O)-S- $R^{40}$ ; wherein when  $R^{25}$  and  $R^{26}$  independently are alkyl or alkoxy,  $R^{25}$  and  $R^{26}$  independently are optionally substituted with one or more moieties selected from the group consisting of cycloalkyl, heterocyclyl, aryl, and heteroaryl; or  $R^{25}$  is -H; and  $R^{26}$  is selected from the group consisting of cycloalkyl, heterocyclyl, aryl, and heteroaryl,  $R^{27}$ ,  $R^{28}$ ,  $R^{29}$ ,  $R^{30}$ ,  $R^{31}$ ,  $R^{32}$ ,  $R^{33}$ ,  $R^{34}$ ,  $R^{35}$ ,  $R^{36}$ ,  $R^{37}$ ,  $R^{38}$ ,  $R^{39}$ , and  $R^{40}$  independently are selected from the group consisting of -H and alkyl, wherein alkyl is optionally substituted by one or more moieties selected from the group consisting of cycloalkyl, heterocyclyl, aryl, and heteroaryl, wherein when any of  $R^{11}$ ,  $R^{12}$ ,  $R^{13}$ ,  $R^{14}$ ,  $R^{15}$ ,  $R^{16}$ ,  $R^{17}$ ,  $R^{18}$ ,  $R^{19}$ ,  $R^{20}$ ,  $R^{21}$ ,  $R^{22}$ ,  $R^{23}$ ,  $R^{24}$ ,  $R^{25}$ ,  $R^{26}$ ,  $R^{27}$ ,  $R^{28}$ ,  $R^{29}$ ,  $R^{30}$ ,  $R^{31}$ ,  $R^{32}$ ,  $R^{33}$ ,  $R^{34}$ ,  $R^{35}$ ,  $R^{36}$ ,  $R^{37}$ ,  $R^{38}$ ,  $R^{39}$ , and  $R^{40}$  independently is a moiety selected from the group consisting of alkyl, alkenyl, alkynyl, alkoxy, alkylthio, cycloalkyl, heterocyclyl, aryl, and heteroaryl, then the moiety is optionally substituted by one or more substituent selected from the group consisting of -OH, alkoxy, and halogen;

a compound represented by Formula III



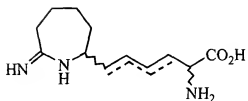
III

wherein:

$R^{41}$  is H or methyl; and

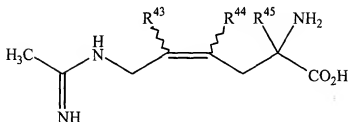
$R^{42}$  is H or methyl;

a compound of formula IV



IV;

5 a compound of Formula V:



V

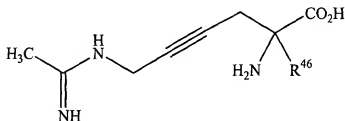
10 wherein:

R<sup>43</sup> is selected from the group consisting of hydrogen, halo, C<sub>1</sub>-C<sub>6</sub> alkyl and C<sub>1</sub>-C<sub>6</sub> alkyl substituted by alkoxy or one or more halo;

R<sup>44</sup> is selected from the group consisting of hydrogen, halo, C<sub>1</sub>-C<sub>6</sub> alkyl and C<sub>1</sub>-C<sub>6</sub> alkyl substituted by alkoxy or one or more halo;

15 R<sup>45</sup> is C<sub>1</sub>-C<sub>6</sub> alkyl or C<sub>1</sub>-C<sub>6</sub> alkyl substituted by alkoxy or one or more halo;

a compound of Formula VI:



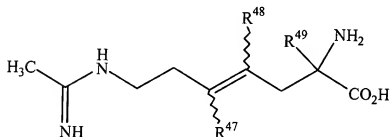
VI

wherein:

$R^{46}$  is  $C_1$ - $C_6$  alkyl, said  $C_1$ - $C_6$  alkyl optionally substituted by halo or alkoxy, said alkoxy optionally substituted by one or more halo;

a compound of Formula VII

5



**VII**

wherein:

10  $R^{47}$  is selected from the group consisting of hydrogen, halo,  $C_1$ - $C_6$  alkyl and  $C_1$ - $C_6$  alkyl substituted by alkoxy or one or more halo;

$R^{48}$  is selected from the group consisting of hydrogen, halo,  $C_1$ - $C_6$  alkyl and  $C_1$ - $C_6$  alkyl substituted by alkoxy or one or more halo;

$R^{49}$  is  $C_1$ - $C_6$  alkyl or  $C_1$ - $C_6$  alkyl be substituted by alkoxy or one or more halo;

15 a compound of Formula VIII

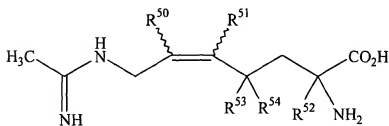


**VIII**

wherein:

$R^{50}$  is  $C_1$ - $C_5$  alkyl, said  $C_1$ - $C_5$  alkyl optionally substituted by halo or alkoxy, said alkoxy optionally substituted by one or more halo;

a compound of formula IX



IX

wherein:

R<sup>50</sup> is selected from the group consisting of hydrogen, halo, and  $C_1$ - $C_5$  alkyl, said  $C_1$ - $C_5$  alkyl optionally substituted by halo or alkoxy, said alkoxy optionally substituted by one or more halo;

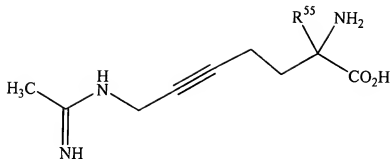
R<sup>51</sup> is selected from the group consisting of hydrogen, halo, and  $C_1$ - $C_5$  alkyl, said  $C_1$ - $C_5$  alkyl optionally substituted by halo or alkoxy, said alkoxy optionally substituted by one or more halo;

R<sup>52</sup> is  $C_1$ - $C_5$  alkyl, said  $C_1$ - $C_5$  alkyl optionally substituted by halo or alkoxy, said alkoxy optionally substituted by one or more halo;

R<sup>53</sup> is selected from the group consisting of hydrogen, halo, and  $C_1$ - $C_5$  alkyl, said  $C_1$ - $C_5$  alkyl optionally substituted by halo or alkoxy, said alkoxy optionally substituted by one or more halo; and

R<sup>54</sup> is selected from the group consisting of halo and  $C_1$ - $C_5$  alkyl, said  $C_1$ - $C_5$  alkyl optionally substituted by halo or alkoxy, said alkoxy optionally substituted by one or more halo;

a compound of formula X

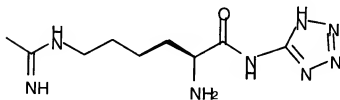


**X**

wherein:

- R<sup>55</sup> is C<sub>1</sub>-C<sub>5</sub> alkyl, said C<sub>1</sub>-C<sub>5</sub> alkyl optionally substituted by halo or alkoxy,  
5 said alkoxy optionally substituted by one or more halo.

*a compound having the formula XI*

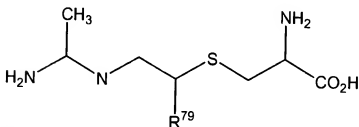


- 10 2S-amino-6-[(1-iminoethyl)amino]-N-(1H-tetrazol-5-yl) hexanamide, hydrate,  
dihydrochloride

**XI**

A compound of formula XII:

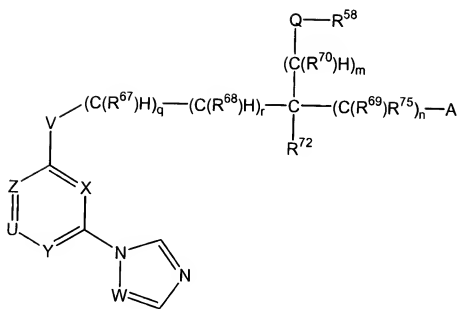
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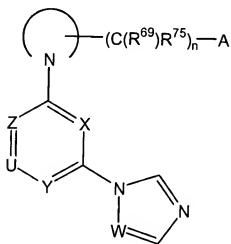
**XII**

- wherein R<sup>79</sup> is selected from C<sub>1-4</sub> alkyl, C<sub>3-4</sub> cycloalkyl, C<sub>1-4</sub> hydroxyalkyl,  
20 and C<sub>1-4</sub> haloalkyl;  
a compound of Formula XIII, Formula XIV or Formula XV:

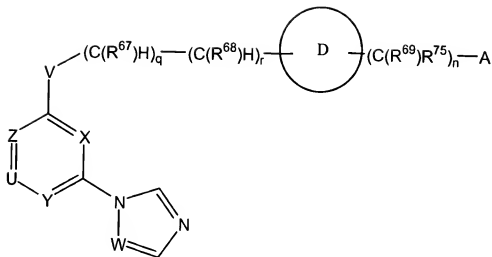




Formula XIII;



Formula XIV; or



Formula XV;

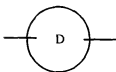
wherein:

- 5 A is  $-R^{56}$ ,  $-OR^{56}$ ,  $C(O)N(R^{56})R^{57}$ ,  $P(O)[N(R^{56})R^{57}]_2$ ,  $-N(R^{56})C(O)R^{57}$ ,  $-N(R^{76})C(O)OR^{56}$ ,  $-N(R^{56})R^{76}$ ,  
 $-N(R^{71})C(O)N(R^{56})R^{71}$ ,  $-S(O)_2R^{56}$ ,  $-SO_2NHC(O)R^{56}$ ,  $-NHSO_2R^{77}$ ,  $-SO_2NH(R^{56})H$ ,  $-C(O)NHSO_2R^{77}$ , and  $-CH=NOR^{56}$ ,  
each X, Y and Z are independently N or  $C(R^{19})$ ;
- 10 each U is N or  $C(R^{60})$ , provided that U is N only when X is N and Z and Y are  $CR^{74}$ ;  
V is  $N(R^{59})$ , S, O or  $C(R^{59})H$ ;  
Each W is N or CH;  
Q is chosen from the group consisting of a direct bond,  $-C(O)-$ ,  $-O-$ ,  $-C(=N-R^{56})-$ ,  
15  $S(O)_2$ , and  $-N(R^{61})-$ ;
- m is zero or an integer from 1 to 4;  
n is zero or an integer from 1 to 3;  
q is zero or one;  
r is zero or one, provided that when Q and V are heteroatoms, m, q, and r  
20 cannot all be zero;

- when A is  $-\text{OR}^{56}$ ,  $\text{N}(\text{R}^{56})\text{C}(\text{O})\text{R}^{57}$ ,  $-\text{N}(\text{R}^{71})\text{C}(\text{O})\text{OR}^{57}$ ,  $-\text{N}(\text{R}^{56})\text{R}^{76}$ ,  $-\text{N}(\text{R}^{71})\text{C}(\text{O})\text{N}(\text{R}^{56})\text{R}^{71}$ ,  $-\text{S}(\text{O})_t\text{R}^{56}$  (where t is zero), or  $-\text{NHSO}_2\text{R}^{77}$ , n, q, and r cannot all be zero; and when Q is a heteroatom and A is  $-\text{OR}^{56}$ ,  $\text{N}(\text{R}^{56})\text{C}(\text{O})\text{R}^{57}$ ,  $-\text{N}(\text{R}^{71})\text{C}(\text{O})\text{OR}^{57}$ ,  $-\text{N}(\text{R}^{56})\text{R}^{76}$ ,  $\text{N}(\text{R}^{71})\text{C}(\text{O})\text{N}(\text{R}^{56})\text{R}^{71}$ ,  $-\text{S}(\text{O})_t\text{R}^{56}$  (when t is zero), or  $-\text{NHSO}_2\text{R}^{77}$ , m and n cannot both be zero; t is zero, one or two;



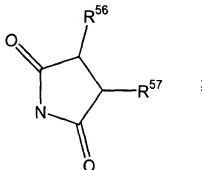
is an optionally substituted N-heterocyclyl;



- 10 is an optionally substituted carbocyclyl or optionally substituted N-heterocyclyl;

- each  $\text{R}^{56}$  and  $\text{R}^{57}$  are independently chosen from the group consisting of hydrogen, optionally substituted  $\text{C}_1\text{-C}_{20}$  alkyl, optionally substituted cycloalkyl,  $-\text{[C}_6\text{-C}_8\text{ alkyl]}\text{-R}^{64}$ ,  $-\text{[C}_2\text{-C}_8\text{ alkenyl]}\text{-R}^{64}$ ,  $-\text{[C}_2\text{-C}_8\text{ alkynyl]}\text{-R}^{64}$ ,  $-\text{[C}_2\text{-C}_8\text{ alkyl]}\text{-R}^{65}$  (optionally substituted by hydroxy),  $-\text{[C}_1\text{-C}_8\text{]}\text{-R}^{66}$  (optionally substituted by hydroxy), optionally substituted heterocyclyl; or  $\text{R}^{56}$  and  $\text{R}^{57}$  together with the nitrogen atom to which they are attached is an optionally substituted N-heterocyclyl;  $\text{R}^{58}$  is chosen from the group consisting of hydrogen, alkyl, cycloalkyl, optionally substituted aryl, haloalkyl,  $-\text{[C}_1\text{-C}_8\text{ alkyl]}\text{-C}(\text{O})\text{N}(\text{R}^{56})\text{R}^{57}$ ,  $-\text{[C}_1\text{-C}_8\text{ alkyl]}\text{-N}(\text{R}^{56})\text{R}^{57}$ ,  $-\text{[C}_1\text{-C}_8\text{ alkyl]}\text{-R}^{63}$ ,  $-\text{[C}_2\text{-C}_8\text{ alk2yl]}\text{-R}^{65}$ ,  $-\text{[C}_1\text{-C}_8\text{ alkyl]}\text{-R}^{66}$ , and heterocyclyl (optionally substituted by one or more substituents selected from the group consisting of halo, alkyl, alkoxy and imidazolyl);
- 20

- or when Q is  $-N(R^{56})-$  or a direct bond to  $R^{56}$ ,  $R^{56}$  may additionally be aminocarbonyl, alkoxy carbonyl, alkylsulfonyl, monoalkylaminocarbonyl, dialkylaminocarbonyl and  $-C(=NR^{73})-NH_2$ ;
- 5 or  $-Q-R^{56}$  taken together represents  $-C(O)OH$ ,  $-C(O)N(R^{56})R^{57}$  or



- $R^{59}$  is chosen from the group consisting of hydrogen, alkyl, aryl, aralkyl and cycloalkyl;
- 10 Provided that when A is  $-R^{56}$  or  $-OR^{56}$ ,  $R^{59}$  cannot be hydrogen, and when V is CH,  $R^{59}$  may additionally be hydroxy;
- $R^{60}$  is chosen from the group consisting of hydrogen, alkyl, aryl, aralkyl, haloalkyl, optionally substituted aralkyl, optionally substituted aryl,  $-OR^{71}$ ,  $-S(O)_2-R^{71}$ ,  $N(R^{71})R^{76}$ ,  $N(R^{71})C(O)N(R^{56})R^{71}$ ,  $N(R^{71})C(O)OR^{71}$ ,  $N(R^{71})C(O)R^{71}$ ,  $-[C_6-C_8 \text{ alkyl}]-C(H)[C(O)R^{71}]_2$  and  $-[C_6-C_8 \text{ alkyl}]-C(O)N(R^{56})R^{71}$ ;
- 15  $R^{61}$  is chosen from the group consisting of hydrogen, alkyl, cycloalkyl,  $-[C_6-C_8 \text{ alkyl}]-R^{63}$ ,  $-[C_2-C_8 \text{ alkyl}]-R^{65}$ ,  $-[C_6-C_8 \text{ alkyl}]-R^{66}$ , acyl,  $-C(O)R^{63}$ ,  $-C(O)-[C_6-C_8 \text{ alkyl}]-R^{63}$ , alkoxy carbonyl, optionally substituted aryloxy carbonyl, optionally substituted aralkoxy carbonyl, alkylsulfonyl, optionally substituted aryl, optionally substituted heterocycl, alkoxy carbonylalkyl, carboxyalkyl, optionally substituted arylsulfonyl, aminocarbonyl, monoalkylaminocarbonyl, dialkylaminocarbonyl, optionally substituted arylaminocarbonyl, aminosulfonyl,
- 20

- monoalkylaminosulfonyl dialkylaminosulfonyl, arylaminosulfonyl, arylsulfonylaminocarbonyl, optionally substituted N-heterocyclyl,  $-C(=NH)-N(CN)R^{56}$ ,  $-C(O)R^{78}-N(R^{56})R^{57}$ ,  $-C(O)-N(R^{56})R^{78}-C(O)OR^{56}$ , each  $R^{63}$  and  $R^{64}$  are independently chosen from the group consisting of
- 5 haloalkyl, cycloalkyl, (optionally substituted with halo, cyano, alkyl or alkoxy), carbocyclyl (optionally substituted with one or more substituents selected from the group consisting of halo, alkyl and alkoxy) and heterocyclyl (optionally substituted with alkyl, aralkyl or alkoxy);
- 10 each  $R^{65}$  is independently chosen from the group consisting of halo, alkoxy, optionally substituted aryloxy, optionally substituted aralkoxy, optionally substituted  $-S(O)_2-R^{77}$ , acylamino, amino, monoalkylamino, dialkylamino, (triphenylmethyl)amino, hydroxy, mercapto, alkylsulfonamido;
- 15 each  $R^{66}$  is independently chosen from the group consisting of cyano, di(alkoxy)alkyl, carboxy, alkoxycarbonyl, aminocarbonyl, monoalkylaminocarbonyl and dialkylaminocarbonyl; each  $R^{67}$ ,  $R^{68}$ ,  $R^{69}$ ,  $R^{70}$ ,  $R^{72}$ , and  $R^{75}$  are independently hydrogen or alkyl;
- 20 each  $R^{71}$  is independently hydrogen, alkyl, optionally substituted aryl, optionally substituted aralkyl or cycloalkyl;  $R^{73}$  is hydrogen,  $NO_2$ , or toluenesulfonyl; each  $R^{74}$  is independently hydrogen, alkyl (optionally substituted with hydroxy), cyclopropyl, halo or haloalkyl;
- 25 each  $R^{76}$  is independently hydrogen, alkyl, cycloalkyl, optionally substituted aryl, optionally substituted aralkyl,  $-C(O)R^{77}$  or  $-SO_2R^{77}$ ; or  $R^{76}$  taken together with  $R^{56}$  and the nitrogen to which they are attached is an optionally

substituted N-heterocyclyl;

or R<sup>76</sup> taken together with R<sup>71</sup> and the nitrogen to which they are attached is an optionally

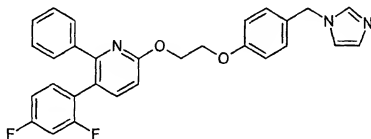
substituted N-heterocyclyl;

- 5 each R<sup>77</sup> is independently alkyl, cycloalkyl, optionally substituted aryl or optionally

substituted aralkyl; and

R<sup>78</sup> is an amino acid residue; and

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- or a pharmaceutically acceptable salt or prodrug of any of said inducible nitric  
15 oxide synthase inhibitors.

23. The method of Claim 22 wherein the antimicrobial compound comprises an antibiotic compound.

20 24. The method of Claim 22 wherein the antimicrobial compound comprises at least one compound selected from the group consisting of the following: amoxicillin, clarithromycin, rifabutin, bismuth subsalicylate, metronidazole, and tetracycline.

25 25. The method of Claim 22 further comprising administering to the subject an amount of an antisecretory compound or pharmaceutically

acceptable salt thereof or prodrug thereof, wherein the amount of the inducible nitric oxide synthase selective inhibitor, the amount of the antibiotic compound and the amount of the antisecretory compound together constitute an amount effective against the condition or disease of the gastrointestinal tract.

5           26. The method of Claim 25 wherein the antisecretory compound comprises a proton-pump inhibitor.

          27. The method of Claim 26 wherein the antisecretory compound comprises omeprazole.

          28. The method of Claim 25 wherein the antisecretory compound  
10 comprises an H<sub>2</sub>receptor anatagonist.

          29. The method of Claim 28 wherein the antisecretory compound comprises ranitidine.

          30. The method of Claim 22 wherein the antimicrobial compound  
comprises a double anti-microbial composition consisting of a combination of  
15 two compounds selected from the group consisting of the following: amoxicillin, clarithromycin, rifabutin, bismuth subsalicylate, metronidazole, and tetracycline.

          31. The method of Claim 22 wherein the condition or disease of the  
gastrointestinal tract is selected from the group consisting of inflammatory  
20 bowel disease, Crohn's disease, ulcerative colitis, peptic ulcer disease, gastric ulceration, duodenal ulceration, esophagitis, gastritis, ileitis, colitis, gastroesophageal reflux disease, irritable bowel syndrome, irritable bowel syndrome, paralytic ileus and diarrhea.

          32. The method of Claim 22 wherein the condition or disease of the  
25 gastrointestinal tract is inflammatory bowel disease.

          33. The method of claim 22 wherein the condition or disease of the  
gastrointestinal tract is Crohn's disease.